UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/445,205	01/07/2000	JEAN-LUC GALZI	97AHCNRFLU	9642

466 7590 12/06/2001

YOUNG & THOMPSON
745 SOUTH 23RD STREET 2ND FLOOR
ARLINGTON, VA 22202

EXAMINER	
SISSON, BRADLEY L	

ART UNIT	PAPER NUMBER
1655	14

DATE MAILED: 12/06/2001

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/445,205	GALZI ET AL.	
	Examiner	Art Unit	
	Bradley L. Sisson	1655	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 August 2001* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *10,12-21,27,28 and 32-35* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *10,12-21,27,28 and 32-35* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Response to Amendment

1. Acknowledgement is made of applicant having filed on 24 August 2001, Paper No. 13, an amendment and Petition for Extension of Time, in response to the letter of 24 July 2001, Paper No. 12. It is noted with particularity that the amendment and petition of Paper No. 13 were unsigned and as such does not constitute a proper amendment. Since the letter of 24 July 2001, Paper No. 12, however, the missing papers for the amendment of 17 July 2001, Paper No. 11, have been located and placed in the file. Accordingly, Paper No. 11, now constitutes a complete response and has been entered.

2. The Office regrets any confusion that may have resulted from the letter of 24 July 2001.

Claim Objections

3. Claims 19 and 28 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form.

4. Claim 19, which depends directly from claim 10, effectively broadens the scope of claim 10 by encompassing the binding of a target protein not in the binding site of a receptor but in alternative sites.

5. Claim 27, the claim from which claim 28 depends, is drawn to a "[p]rocess for detecting and quantifying...." Claim 28 effectively broadens the scope by requiring that one "possibly quantify interactions" (emphasis added).

Claim Rejections - 35 USC § 112

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 10-21, 27, 28 and 32-35 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. See the Office action of 17 January 2001 for the basis of the rejection.

8. Claims 10-21, 27, 28, and 32-35 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. See the Office action of 17 January 2001 for the basis of the rejection.

Response to argument

Acknowledgement is made at pages 17-22 of the response of 17 July 2001 (and 24 August 2001) that the written description requirement is met by the aspect that the disclosure is an original (page 7); that applicant has enabled the invention by way of the disclosure, including

four examples; and that these examples show that applicant was in possession of several variants of GFP (EGFP, ECFP, and EYFP).

The above arguments and accompanying showings have been fully considered and have not been found persuasive towards the withdrawal of the rejection, nor to save new claim 35 from being similarly rejected. While agreement is reached in that an applicant need not set forth each and every possible of a method nor describe each and every species encompassed by a generic claim, the specification must adequately describe that applicant was in possession of the invention at the time of filing. The claimed method encompasses and in fact explicitly states that one can use any number of possible variants of GFP as well as "fluorescence substance." The variants of GFP as well as the use of GFP required in at least one embodiment, that one have operably linked and expressed constructs of fusion proteins. In view of the claims encompassing genetic variants and fragments that "conserve the fluorescence property," the specification must provide an adequate written description of the species encompassed by these generic claims. It is noted that the method claims are not directed to a method of finding or producing the fusion proteins but are directed to their use. Accordingly, the reagents needed for practicing the methods must be available, else, the skilled artisan will have to resort to in making reagents and determining how, if at all, they are to be used. Such non-disclosure on the part of applicant unfairly shifts the burden of enablement to that of the public to the point that it constitutes undue experimentation. *Genentech v. Novo Nordisk A/S* 42 USPQ2d 1001.

It is well settled that one cannot enable the use of compounds not in their possession. *Fiers v. Sugano* 25 USPQ2d 1604-5 (CAFC, January 1993). In the case of claims 32-34, drawn to a kit that comprises such variants, the claims have been found to encompass any and all

possible variants that "conserve the fluorescence property." While argument has been presented that the specification sets forth three variants of GFP, such a showing is not considered to be sufficient given the size of the genus of proteins that is considered to number into the thousands. In support of this position, attention is directed to the decision in *In re Shokal*, 113 USPQ 283 (CCPA 1957) wherein is stated:

> It appears to be well settled that a single species can rarely, if ever, afford sufficient support for a generic claim. In re Soll, 25 C.C.P.A. (Patents) 1309, 97 F.2d 623, 38 USPQ 189; In re Wahlforss et al., 28 C.C.P.A. (Patents) 867, 117 F.2d 270, 48 USPQ 397. The decisions do not however fix any definite number of species which will establish completion of a generic invention and it seems evident therefrom that such number will vary, depending on the circumstances of particular cases. Thus, in the case of small genus such as the halogens, consisting of four species, a reduction to practice of three, or perhaps even two, might serve to complete the generic invention, while in the case of a genus comprising hundreds of species, a considerably larger number of reductions to practice would probably be necessary. (emphasis added)
>
> ***
>
> We are of the opinion that a genus containing such a large number of species cannot properly be identified by the mere recitation or reduction to practice of four or five of them. As was pointed out by the examiner, four species might be held to support a genus, if such genus is disclosed in clear language; but where those species must be relied on not only to illustrate the genus but to define what it is, the situation is otherwise.

For the above reasons, and in the absence of convincing evidence to the contrary, the rejection is maintained.

9. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

10. Claims 10 12-21, 27, 28, and 32-35 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

11. Claim 10 is confusing where in lines 4-5 it is stated:

> ...cells or cell fragments are prepared containing a DNA sequence comprising a gene coding for a fluorescent protein fused with a gene for the target protein....

It is unclear if the cells and cell-fragments are to comprise the DNA construct or whether this is to be added as a result of the step. It is also unclear whether the construct must have been expressed in the cell, or in the cell fragments so that the fusion protein is present. Alternatively, is the fusion protein simply added later?

12. Claim 10, line 23, is indefinite with respect to just what is labeled. In particular, is the label bound to: 1) the cell or cell fragment; 2) the target protein; or 3) the ligand?

13. Claim 10 recites the limitation "the receptor" in line 11. There is insufficient antecedent basis for this limitation in the claim.

14. Claim 10, penultimate indentation, is confusing as to what purpose, if any, prior irradiation has on cells and cell fragments. Is this "irradiation" to be at a wavelength that will excite the fluorescent protein and/or the fluorescent substance, or does irradiating with white light suffice? Additionally, it would appear that one would need to record and compare signals generated so to arrive at the required decision point of determining whether or not a reduction in an amplitude and/or emission signal has occurred. It is unclear how one determines if there has been a reduction in amplitude and/or emission signal when only one irradiation is required. Seemingly the method of claim 10 is missing essential method steps.

15. Claims 10-21 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: Those that will result in the quantification of the non-covalent interactions. As presently worded, the claim is to result in the "detection and quantification of non-covalent interactions. The method steps, however, only result in the detection of a fluorescent signal. No correlation is required to be made between the signal(s) and any interaction, much less a quantification of the (various) interactions.

16. Claim 12 is indefinite with respect to recitation of "a ligand." Is the "ligand" the same as or different from the "ligand" of claim 10? If it is different, in what manner is it different?

17. Claim 12 recites the limitation "the above-mentioned non-labeled ligand" in line 11. There is insufficient antecedent basis for this limitation in the claim.

18. Claim 12 is confusing as a result of the phrase "and of a ligand"; see e.g., lines 4 and 7.

19. Claim 12 is confusing as a result of the phrase in the last indentation which reads in part: "the reductions in the amplitude of the donor's emission." Such language would seemingly be indicating that there would be more than one reduction but just what the plurality of entities that re to undergo a reduction is not clear. Also in the same indentation, there also seem to be a plurality of emission spectra with respect to acceptor's emission.

20. Claim 14, last indentation, is indefinite with respect to just constitutes the threshold for a compound to meet the test for being "structurally linked." For purposes of examination the phase has been interpreted as meaning that there is a structural similarity, not that there is a physical linkage. If perhaps the interpretation of the phrase is incorrect, applicant is requested to clearly state on the record what the intent of the phrase is.

21. Claims 15 and 16 lack antecedent support for the phrase "the energy transfer."

22. Claim 15 lacks antecedent support for the phrase "the emission signal of Bodipy," "the irradiation wavelength" and "the excitation wavelength of EGFP."

23. Claim 19 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: those steps that result in "detecting and quantifying non-covalent interactions between a target protein and one of its ligands" where said target protein-ligand interaction does not take place at a binding site but in the "first or third intracellular loop of the receptor."

24. Regarding claim 20, the phrase "such as" renders the claim indefinite because it is unclear whether the limitations following the phrase are part of the claimed invention. See MPEP § 2173.05(d).

25. Claim 21 recites the limitation "the same pharmacological specificity" in lines 5-6. There is insufficient antecedent basis for this limitation in the claim.

26. Claim 21 recites the limitation "the signal/.noise ratio" in line 6. There is insufficient antecedent basis for this limitation in the claim.

27. Claim 27 recites the limitation "the G proteins" in line 2. There is insufficient antecedent basis for this limitation in the claim.

28. Claim 27 recites the limitation "the response transduction function" in line 16. There is insufficient antecedent basis for this limitation in the claim.

29. Claim 27 is confusing as a result of the phrase "labeled with a labeled;" see line 29.

30. Claims 27 and 28 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: Those that will result in the quantification and identification of any and all non-covalent interactions between any target protein (receptor) and protein G, e.g., see claim 19. As presently worded, claim 27 sets forth a description of the type of interactions but does not state positive method steeps by which they are to be achieved. At best, claim 27 can be argued as requiring the detection of a signal. Just how a signal is to be transformed or correlated into the detection and quantification of any and all non-covalent interactions encompassed by the claim is less than clear.

31. Claims 33 and 34 are confusing as a result of the usage of "(No 1)" and "(No 2)." It is unclear if this is to be interpreted as a parenthetical expression, e.g., --a first fluorescent protein-- or whether it is in reference to something else. Clarification is requested.

32. Claim 33 is confusing as a result of the expression "or;". Seemingly a comma, not a semicolon, should follow the alternative. It is unclear if some other meaning is to be applied here.

33. Claims 10-35 are indefinite with respect to "the fluorescence property." Is "the fluorescence property" that of GFP, a variant thereof, or is it a property common to some or all fluorescent compounds?

34. Claim 35 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: Those that will result in the quantification of the non-covalent interactions. As presently worded, the claim is to result in the "detection and quantification of

non-covalent interactions. The method steps, however, only result in the detection of a fluorescent signal. No correlation is required to be made between the signal(s) and any interaction, much less a quantification of the (various) interactions.

Conclusion

35. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bradley L. Sisson whose telephone number is 703-308-3978. The examiner can normally be reached on Monday through Thursday from 6:30 AM to 5 PM.

36. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, W. Gary Jones can be reached on 703-308-1152. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3592 for regular communications and 703-308-0294 for After Final communications.

37. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1234.

B. L. Sisson

Bradley L. Sisson
Primary Examiner
Art Unit 1655

bls
December 2, 2001